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51

1.-25. (canceled)

26. A method of halogenating a complex organic compound comprising contacting a complex organic compound with a flavin-dependent halogenase (FDH) variant comprising one or two amino acid substitutions compared to the amino acid sequence set forth in SEQ ID NO:2 or SEQ ID NO:4, wherein the FDH variant is capable of catalyzing the halogenation of a complex organic compound and a halogen under conditions suitable for enzyme-catalyzed halogenation of the complex organic compound.

27. The method of claim **26** wherein the complex organic compound is an aromatic heterocyclic organic compound.

28. The method of claim **27** wherein the aromatic heterocyclic organic compound comprises a bicyclo[2.2.2]diazaoctane ring.

29. The method of claim **27** wherein the aromatic heterocyclic organic compound comprises indole.

30. The method of claim **29** wherein the compound is an indole alkaloid.

31. The method of claim **30** wherein the indole alkaloid is a prenylated indole alkaloid.

32. The method of claim **31** wherein the prenylated indole alkaloid is derived from a *Malbranchea* species.

33. The method of claim **32** wherein the *Malbranchea* species is *Malbranchea aurantiaca* or *Malbranchea graminicola*.

34. The method of claim **31** wherein the prenylated indole alkaloid is premalbrancheamide, malbrancheamide B, iso-malbrancheamide B, malbrancheamide C, or isomalbrancheamide C.

35. The method of claim **26** wherein the halogenation step is a chlorination step.

36. The method of claim **26** wherein the halogenation step is a bromination step.

37. A method of modulating a Ca²⁺ signaling pathway in a cell of a mammal comprising administering an effective amount of a halogenated complex organic compound to the mammal.

38. The method of claim **37** wherein the Ca²⁺ signaling pathway is a Ca²⁺-calmodulin dependent pathway.

39. The method of claim **37** wherein modulating the Ca²⁺ signaling pathway inhibits smooth muscle contraction.

40. The method of claim **37** wherein the halogenated complex organic compound is malbrancheamide, malbrancheamide B, isomalbrancheamide B, malbrancheamide C, isomalbrancheamide C, malbrancheamide D, isomalbrancheamide D, or malbrancheamide

41. A method of modulating a Ca²⁺ signaling pathway in a cell in vitro or in an isolated enzyme or enzymes in vitro comprising administering an effective amount of a halogenated complex organic compound to the cell in vitro or to the isolated enzyme or enzymes in vitro.

42. The method of claim **41** wherein the Ca²⁺ signaling pathway is a Ca²⁺-calmodulin dependent pathway.